

IN THE CLAIMS

The following listing of claims will replace all prior versions, and listing of claims, in this application:

1. (Currently Amended) A method of producing a lysosomal hydrolase having an oligosaccharide modified with N-acetylglucosamineacetylglucosamine-1-phosphate comprising
 - a. contacting a mammalian cell culture expressing a lysosomal hydrolase with a mutagenic agent;
 - b. culturing said mammalian cell culture in the presence of *Pseudomonas* exotoxin A in an amount sufficient to select for cells resistant to the *Pseudomonas* exotoxin A;
 - c. selecting said cells resistant to *Pseudomonas* exotoxin A; and
 - d. isolating said lysosomal hydrolase having an N-acetylglucosamineacetylglucosamine-1-phosphate from said resistant cells.
2. (Currently Amended) The method of Claim 1, wherein said lysosomal hydrolase is selected from the group consisting of α -glucosidase, α -L-iduronidase, α -galactosidase A, arylsulfatase, N-acetylgalactosamine-6-sulfatase, α -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase, β -glucuronidase, Heparan N-sulfatase, N-Acetyl- α -glucosaminidase, Acetyl CoA- α -glucosaminide N-acetyl transferase, N-acetyl-glucosamine-6 sulfatase, Galactose 6-sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, ~~Arylsulfatase A~~ ~~Cerebrosidase~~, Ganglioside sialidase, Acid β -galactosidase G_{M1} Galgliside, Acid β -galactosidase, Hexosaminidase A, Hexosaminidase B, α -fucosidase, α -N-Acetyl galactosaminidase, Glycoprotein Neuraminidase, Aspartylglucosamine amidase,

Acid Lipase, Acid Ceramidase, Lysosomal Sphingomyelinase and
Sphingomyelinase.

3. (Currently Amended) The method of Claim 1, further comprising contacting said lysosomal hydrolase having an ~~N-acetylglucosamine~~N-acetylglucosamine-1-phosphate with an active ~~GlcNAc-phosphotransferase~~N-acetylglucosamine-1-phosphodiester α N-acetyl glucosimanidase.
4. (Currently Amended) The method of Claim 3, wherein said ~~phosphodiester α -GlcNAc~~N-acetylglucosamine-1-phosphodiester α N-acetyl glucosimanidase comprises an amino acid ~~acids~~56 to 515 of SEQ ID NO:18.
5. (Currently Amended) The method of Claim 3, wherein said ~~phosphodiester α -GlcNAc~~N-acetylglucosamine-1-phosphodiester α N-acetyl glucosimanidase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.
6. (Currently Amended) The method of Claim 3, further comprising purifying said ~~glycoprotein~~lysosomal hydrolase after said contacting.
7. (Original) The method of Claim 1, wherein said mutagenic agent is a chemical mutagenic agent.
8. (Original) The method of Claim 7, wherein said mutagenic agent is ethyl methane sulfonate.
9. (Original) The method of Claim 1, further comprises culturing said mammalian cell culture in the presence of a α 1,2-mannosidase inhibitor.
10. (Original) The method of Claim 9, wherein said a α 1,2-mannosidase inhibitor comprises both deoxymannojirimycin and kifunensine.

11. (Withdrawn) ~~A~~ The method of producing a lysosomal hydrolase having an oligosaccharide modified with N-acetylglucosamine-1-phosphate Claim 1, further comprising
- ~~a.~~ introducing a polynucleotide sequence encoding the lysosomal hydrolase in the cells resistant to *Pseudomonas* exotoxin A before said isolating said lysosomal hydrolase a furin-deficient mammalian cell;
 - ~~b.~~ culturing said furin-deficient mammalian cell containing the polynucleotide sequence encoding the lysosomal hydrolase for a time and under conditions suitable for expression of the lysosomal hydrolase; and
 - ~~c.~~ collecting the lysosomal hydrolase expressed.
12. (Withdrawn) The method of Claim 11, wherein said lysosomal hydrolase is selected from the group consisting of α -glucosidase, α -L-iduronidase, α -galactosidase A, arylsulfatase, N-acetylgalactosamine-6-sulfatase or β -galactosidase, iduronate 2-sulfatase, ceramidase, galactocerebrosidase, β -glucuronidase, Heparan N-sulfatase, N-Acetyl- α -glucosaminidase, Acetyl CoA- α -glucosaminide N-acetyl transferase, N-acetyl-glucosamine-6 sulfatase, Galactose 6-sulfatase, Arylsulfatase A, Arylsulfatase B, Arylsulfatase C, Arylsulfatase A Cerebroside, Ganglioside, Acid β -galactosidase G_{M1} Galglioside, Acid β -galactosidase, Hexosaminidase A, Hexosaminidase B, α -fucosidase, α -N-Acetyl galactosaminidase, Glycoprotein Neuraminidase, Aspartylglucosamine amidase, Acid Lipase, Acid Ceramidase, Lysosomal Sphingomyelinase and Sphingomyelinase.
13. (Withdrawn) The method of Claim 11, further comprising contacting said lysosomal hydrolase having an N-~~acetylglucosamine~~ acetylglucosamine-1-

phosphate with an active ~~GlcNAc-phosphotransferase~~ N-acetylglucosamine-1-phosphodiester α N-acetyl glucosimanidase.

14. (Withdrawn) The method of Claim 13, wherein said ~~phosphodiester α GlcNAcase~~ N-acetylglucosamine-1-phosphodiester α N-acetyl glucosimanidase comprises an amino acids 56 to 515 of SEQ ID NO:18.
15. (Withdrawn) The method of Claim 13, wherein said ~~phosphodiester α GlcNAcase~~ N-acetylglucosamine-1-phosphodiester α N-acetyl glucosimanidase is encoded by a nucleotide sequence comprising SEQ ID NO:17 or a nucleotide sequence that hybridizes under stringent conditions to the complement of SEQ ID NO:17.
16. (Withdrawn) The method of Claim 13, further comprising purifying said ~~glycoprotein~~ lysosomal hydrolase after said contacting.
17. (Withdrawn) The method of Claim 11, further comprises culturing said mammalian cell culture in the presence of a α 1,2-mannosidase inhibitor.
18. (Withdrawn) The method of Claim 17, wherein said a α 1,2-mannosidase inhibitor comprises both deoxymannojirimycin and kifunensine.

Claims 19-44 (Cancelled).

45. (New) An isolated lysosomal hydrolase produced by the method of Claim 1.
46. (New) An isolated lysosomal hydrolase produced by the method of Claim 2.
47. (New) An isolated lysosomal hydrolase produced by the method of Claim 3.
48. (New) An isolated lysosomal hydrolase produced by the method of Claim 4.
49. (New) An isolated lysosomal hydrolase produced by the method of Claim 5.
50. (New) An isolated lysosomal hydrolase produced by the method of Claim 6.
51. (New) An isolated lysosomal hydrolase produced by the method of Claim 7.
52. (New) An isolated lysosomal hydrolase produced by the method of Claim 8.
53. (New) An isolated lysosomal hydrolase produced by the method of Claim 9.

- 54. (New) An isolated lysosomal hydrolase produced by the method of Claim 10.
- 55. (New) An isolated lysosomal hydrolase produced by the method of Claim 11.
- 56. (New) An isolated lysosomal hydrolase produced by the method of Claim 12.
- 57. (New) An isolated lysosomal hydrolase produced by the method of Claim 13.
- 58. (New) An isolated lysosomal hydrolase produced by the method of Claim 14.
- 59. (New) An isolated lysosomal hydrolase produced by the method of Claim 15.
- 60. (New) An isolated lysosomal hydrolase produced by the method of Claim 16.
- 61. (New) An isolated lysosomal hydrolase produced by the method of Claim 17.
- 62. (New) An isolated lysosomal hydrolase produced by the method of Claim 18.